

Figure 1: Human IRS-1 protein sequence (SEQ ID NO: 1)

1 masppesdgp sdvrkvgylr kpksmhkrrf vlaaseagg parleyyene kkwrhkssap
61 krsiplescf ninkradskn khlvalytrd ehfaiaadse aeqdswyqal lqlhnarakgh
5 121 hdgaaalgag ggggscsgss glgeagedls ygdvppgpaf kevwqvilkp kglgqtknli
181 giyrlcltsk tisfvklnse aaavvlqlmn irrcghsenf ffievgrsav tgpgefwmqv
241 ddsvvaqnmh etileamram sdefrprsks qsssncsnpi svplrrhhln npppsqvglt
301 rrsrtesita tspasmvggk pgsfrvrass dgegtmsrpa svdgspvsps tnrthahrhr
361 gsarlhppln hsrsipmpas rcspusatpvc slsssstsgh gstsdcclfpr rssasvsgsp
10 421 sdggfissde ygsspcdftrs sfrsvtpdsl ghtppargee elsnyicmgg kgpstltapn
481 ghyilsrggn ghrctptglt gtspalagde aasaadldnr frkrthsagt sptithqktp
541 sqssvasiee ytemmpaypp gggsggrlpg hrhsafvptr sypeeglemh plerrgghhr
601 pdsstlhtdd gympmspgva pvpngrkgsg dympmspkv sapqqiinpi rrhpqrwdpn
661 gymmmmspsgg cspdiggps sssssnavp sgtsygklwt ngvgghhshv lphpkppves
15 721 sggkllpctg dynmnmspvgd sntsspsdcy ygpedpqhkp vlsyyislprs fkhtqrgep
781 eegarhqhlr ldstssgrlly aataddssss tssdlslggyy cgarlepslp hphhqvlqph
841 lprkvdttaaq tnsrlarptr lslgdpkast lprareqqqq qqpllhpppep kspgeyvnne
901 fgasdqsgyls gpvafhssps vrcpsqlqpa preeetgee ymkmdlgpgr raawqestgv
961 emgrlgpapp gaasicrptr avpssrgdym tmqmscprqs yvdtspaapv syadmrtgia
20 1021 aeevslprat maaassssaa sasptgpqga aelaahssll ggpqgpggms aftrvnlsrn
1081 rnqsakvira dpqgcrrrhs **setfsst**psa trvgntvpgf agaavggggg sssssedvkr
1141 hssasfenvw lrpgelggap kepaklcgaa gglenglnyi dldlvkdfkq cpqectpepq
1201 ppppppphpqp lgsgessstr rssedlsaya sisfqkqped rq

Figure 2: Human IRS-2 protein sequence (SEQ ID NO: 2)

1 maspprhgpp gpasgdgpnl nnnnnnnnhs vrkcgylrkq khghkrffvl rgpgaggdka
61 tagggsapqp prleyyesek nwrskagapk rvialdccln inkradpkhk ylialytkde
121 yfavaaaeneq eqegwyralt dlvsegrraaa gdappaaapa ascsaslpga vggsgagaaga
5 181 edsyglvapa taayrevwqv nlkpklgqs knltgvrylc lsartigfvk lnceqpsvtl
241 qlmnirrcgh sdsfflievg rsavtgp gel wmqaddsvva qnihetilea mkalkelfef
301 rprsksqssg ssathpisvp garrhhhlnv lppsqtgtlvr rsrtdslaat ppaakcsscr
361 vrtasegdgg aaagaaaaaga rpvsvagspl spgpvraps rshtliggcr aagtktwhcfc
421 aggglqhsrs msmpvehlpp aatspgslss ssdhgwgsyp pppgphpllp hplhhgpgqr
10 481 pssgsasasg spsdpgfmsl deygsspgdl rafcshrsnt pesiaeetppa rdgggggefy
541 gymtmdrpls hcgrsyrrvs gdaaqdldrg lkrkrtysltt parqrpvlpq ssasldeyt
601 mratfsgsag rlcpscpass pkvayhpype dyggdieigsh rssssnlgad dgympmtpga
661 alagsgsgsc rsddymppmsp asvsapkql qpraaaaaaaa avpfagpagp aptfaagrtf
721 pasgggykas spaesspeds gymrmwcgsk lsmehadgkl lpngdylnvs psdavttgtp
15 781 pdffsaalhp ggeplrgvpg ccyclprsy kapytcggds dqyvlmssp v grileeerle
841 pqatpgptqa asafgagptq pphpvvpspv rpsgrpegf lgqrgravrp trlsleglps
901 lpsmheyplp pepkspgeyi nidfgepgar lappapllsa saasssslls asspalslgs
961 gtpgtssdsr qrsplsdymn ldfsspkspk pgapsghpvg sldgllspea sspypplppr
1021 psaspssslq ppppppapge lyrlppasav ataqqgpaas slssdtgdng dytemafgva
20 1081 atppqpliaap pkpeaarvas ptsgvkrlsl meqvsgveaf lqasqppdph rgakviradp
1141 qggrrrhsse tfssttvtp vspsfahnpk rhnsasvenv slrksseggv gvgpgggdep
1201 ptsprqlqpa pplapqgrp w tpgqpgglvg cpgsggspmr retsagfqng lkyiaidvre
1261 epglppqppq pppplpqpgd ksswgrtrsl gglisavgvg strggcggpg pgapapcptt
1321 yaqh

Figure 3: Serine phosphorylation of IRS-1 in CHO/IR/IRS-1 cells

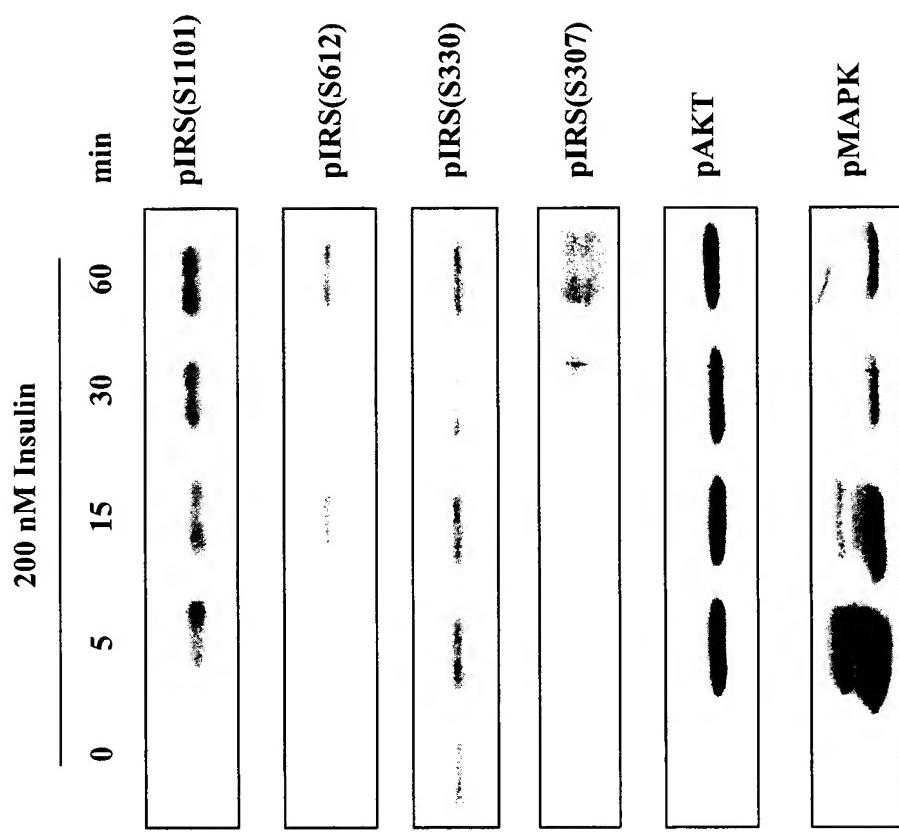


Figure 4: Phosphorylation of IRS-1 in 3T3L1 fat cells

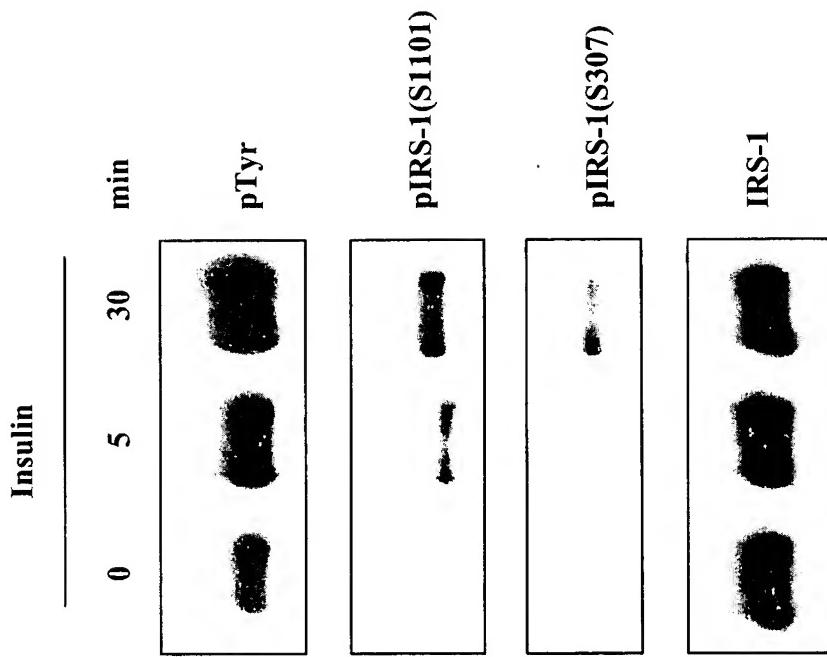


Figure 5: Phosphorylation of IRS-1 in L6 myocytes

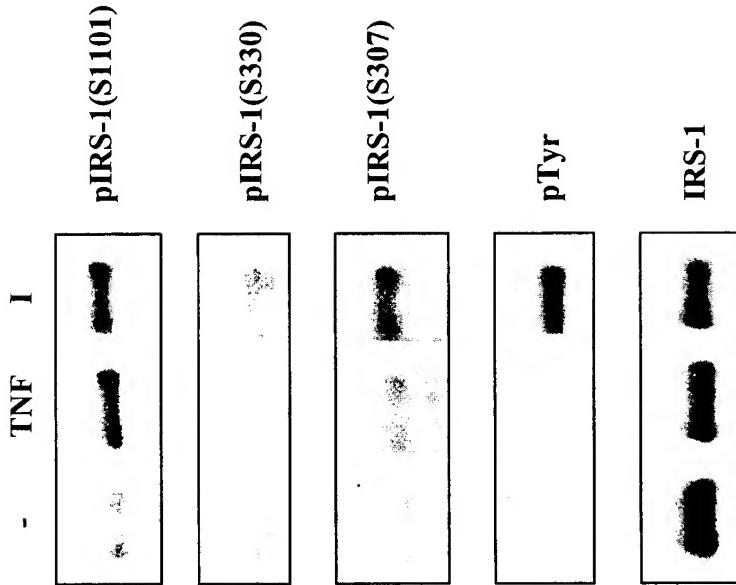


Figure 6: Specificity of pIRS-1(Ser1101) antibody

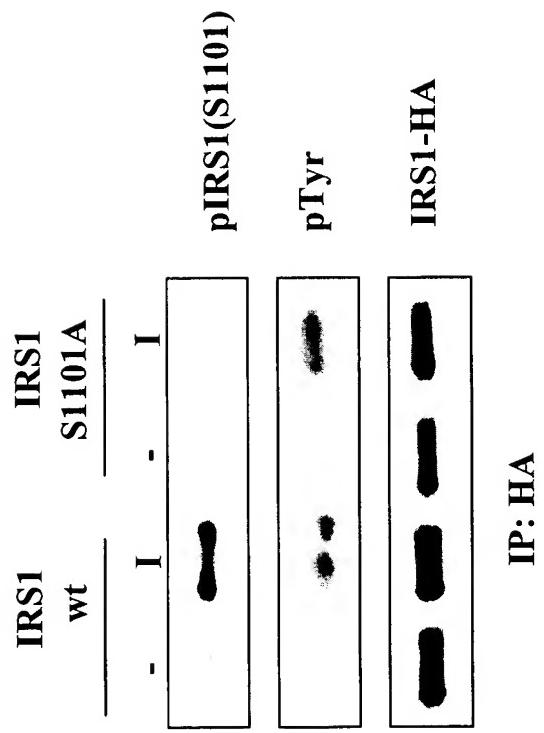
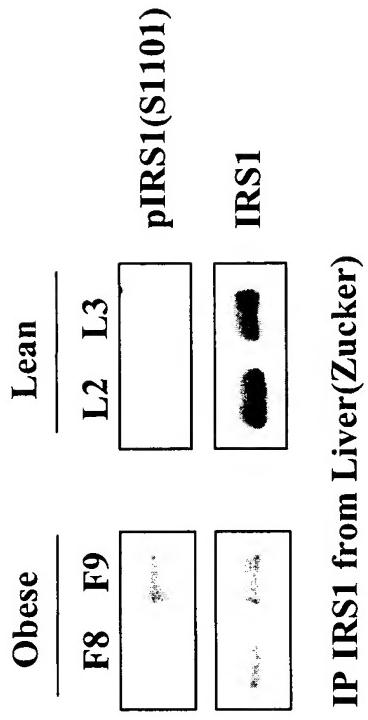


Figure 7: Phosphorylation of IRS-1 at Ser1101 in liver of Zucker rats



IP IRS1 from Liver(Zucker)

Figure 8: Phosphorylation of IRS-2 at Ser1149 in CHO cells

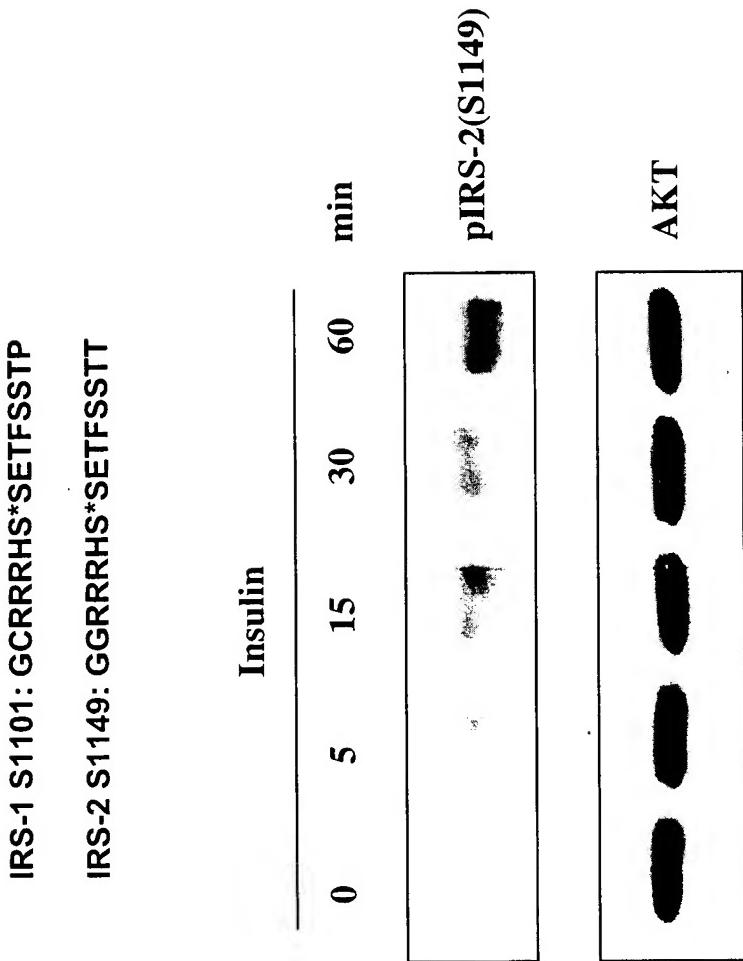


Figure 9: Phosphorylation of IRS1 at Ser1101 correlates with PKC activation

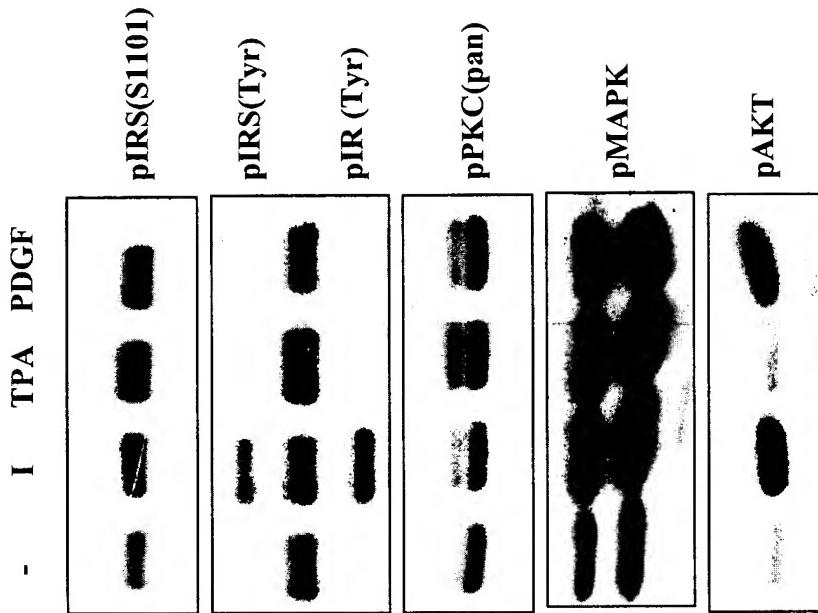


Figure 10: Phosphorylation of IRS1 at Ser1101 is blocked by PKC inhibition

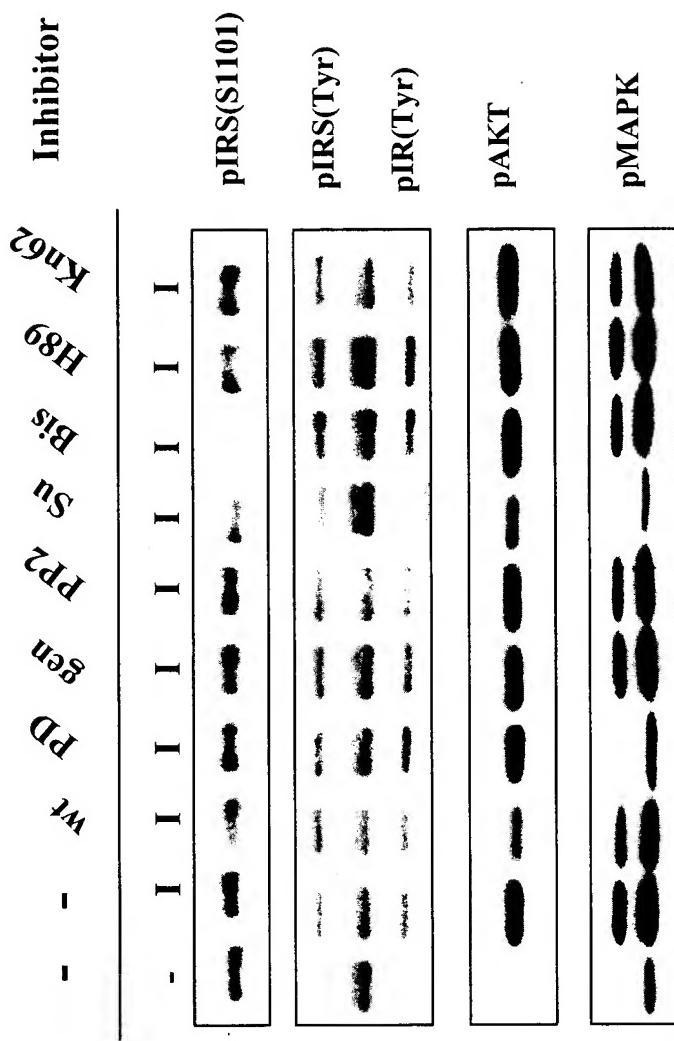


Figure 12: PKC θ kinase phosphorylates IRS-1(Ser1101) in vivo

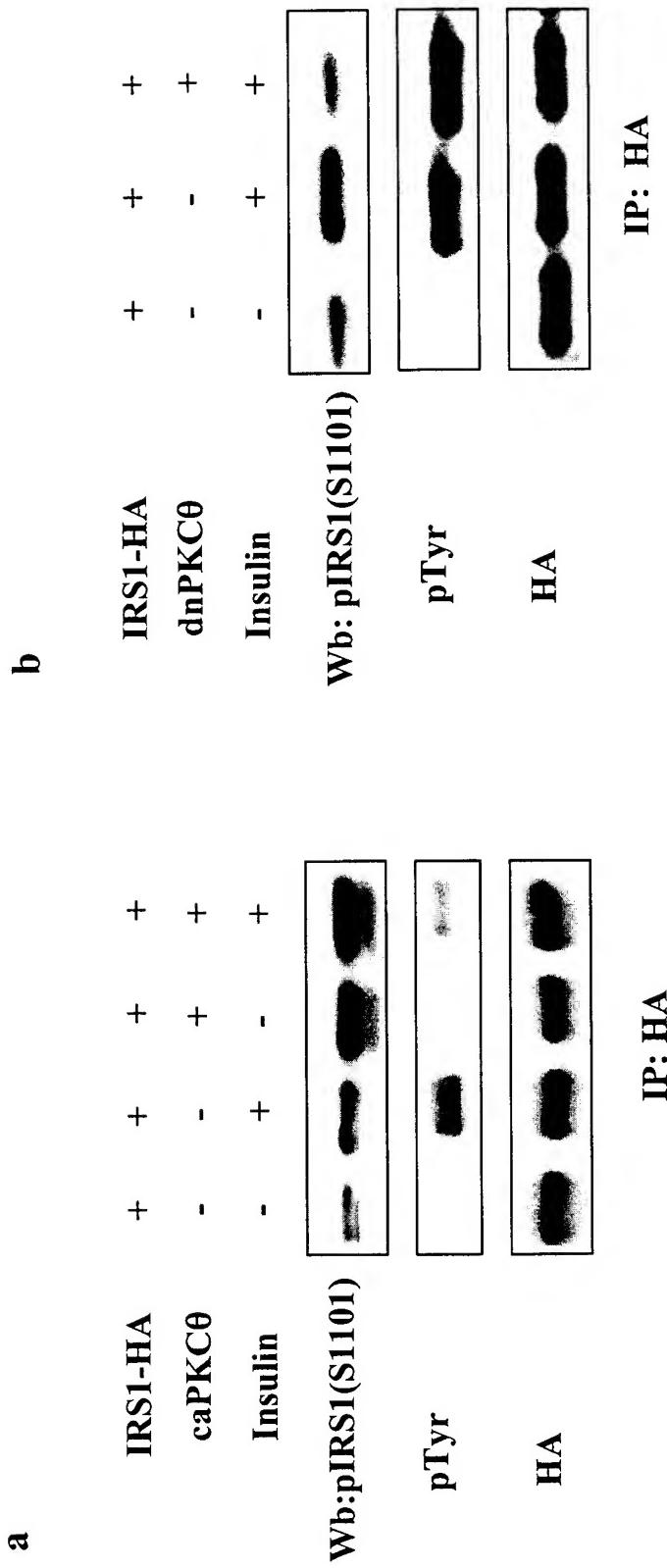


Figure 13: Mouse IRS-1 protein sequence (SEQ ID NO: 3)

1 masppdtfdf sdvrkvgylr kpksmhkrrf vlriraaseagg parleyyene kkwrhkssap
61 krsiplescf ninkradskn khlvallytrd ehfaiaadse aeqdswyqal lqlhnarakah
121 hdgagggcgg scsgssgvge agedlsydtg pgpafkevwq vilkpklgq tknligiyrl
181 cltsktisfv klnseaaavv lqlmnirrcg hsenfffiev grsavtgpge fwmqvddsvv
241 aqnmhetile amramsdefr prsksqssss csnpisvplr rhhlnnpps qvglrrsrt
301 esitatspas mvggkpgsfr vrassdgegt msrpasvdgs pvspstnrt hhrhrgssrl
361 hpplnhsrsi pmrssrcsps atspvsllss stsghgstd clfprrssas vsgspsdggf
421 issdeygssp cdfrssfrsv tpdslghtpp argeeelsny icmggkgast laapnghyil
481 srggnghryi pganlgtspa lpgdeaagaa dldnfrkrts hsagtspis hqktpsqssv
541 asieeytemm paayppgggs ggrlpgyrhs afvpthsype eglemhller rgghhrpdts
601 nlhtddgymp mspgvapvps nrkgngdymp mspksvsapq qiiinpirrhp qrvdpngymmm
661 mspsgscspd igggssssssisaapsgssy gkpwtngvvg hhthalphak ppvesggkl
721 lpctgdymnm spvgdsntss psecyygped pqhkpvlisy slprsfkhtq rpgepeegar
781 hqhrlssss grlrytatae dsssstssds lgggycgar esslthphhh vlqphlprkv
841 dtaaqttsrl arptrlsgd pkastlprvr eqqqqqqssl hppepkspge yvniefgsgq
901 pgylagpats rsspsvrcpp qlhpapreet gseeymnmdl gpgrratwqe sggvelgrig
961 pappgsatvc rptrvpnnsr gdymtmqigc prqsyvdtsp vapvsysadmr tgiaaekasl
1021 prptgaappp sstasssvtp qgataeqath ssllggpqgp ggmsafrvn lspnhnqsak
1081 viradtagcr **rrhssetfsa** ptragntvpf gagaavggsg ggggggsedv krhssasfen
1141 vwlrpgdlgg vskesapvcg aaggleksln yiddlaker sqdcpsqqqs lppppphqpl
1201 gsnegnsprr ssedlsnyas isfqkqpqpedr q

Figure 14: Mouse IRS-2 protein sequence (SEQ ID NO: 4)

1 masaplgppp asgggdgpnl nnnnnnnnhs vrkgcylrkq khghkrffvl rgpgtggdea
61 saaggsppqp prleyyesek kwrskagapk rvialdccln inkradakhk ylialytkde
121 yfavaaeneq eeqegwyralt dlvsegrsge ggsgttggsc saslpvgvlgg sagaagcddn
181 yglvtpatav yrevwqvnlk pkglgqsknl tgvyrlcsa rtigfvklnc egpsvtlqln
241 nirrcghsds fffievgrsa vtgpgelwmq addsvvaqni hetileamka lkelfefrpr
301 sksqssgssa thpisvpgar rhhhlnlpp sqtgtvrrsr tdslaatppa akctscrvt
361 asegdggaaag gagtaggrpm svagsplspg pvrapsrsh tisagcggrp skvtlapagg
421 alqhsrsnsm pvahtsppaat spgslssssg hgsgsyplpp gshphlphpl hhpqgqrpss
481 gsasasgsps dpgfmsldey gsspgdlraf sshrsntpes iaetppardg sggelygym
541 mdrplshcgr pyrrvsgdga qdldrglkrk tyslttparq rqvpqpssas ldeytlmrat
601 fsgssgrlcsp sfpasppkva ynpypedygd ieigshksss snlgaddgym pmtpgaalrs
661 ggpnscsksdd ympmsptsvs apkqilqprl aaalppsgaa vpappsgvgr tfpvnggyk
721 asspaesspe dsgymrmwcg sklsmenpdः kllpngdyln kspseagttag tppdfaalar
781 ggseglkgip ghcysslprs ykapcscsgd ndqyvilmssp vgrileerl epqatpgagt
841 fgaaggshfq phhsavpssm rpsaiggrpe gflgqrcrav rptrlslegl qtipsmqeyp
901 lptepkspge yinidpgeag trlsppappl lasaassssl lsasspassl gsgtptgssd
961 srqrspisdy mnldpsspkp pkpstrsgdt vgsmdgllsp easspypplp prpstspssi
1021 qqplppapgd lyrllppasaa tsqqptagss mssepgdngd ysemafgvaa tppqpvivapp
1081 kpegarvasp tsglkrisl dqvsgveafl qvsqppdphr gakviradpq **ggrrrhssset**
1141 **fsstttvtpv** spsfahnskr hnsasvenvs lrkssegsst lgggdeppts pgqaqplvav
1201 ppvpqarpwn pgqpgaligc pggssspmr etsvgfqngl nyiaidvrge qgslaqsqpp
1261 pgdknswsrt rslggllgtv ggsgasgvvcg gpgtgalpsa styasidfls hhlkeatvvk
1321 e